AD_____

Award Number: DAMD17-99-1-9391

TITLE: MRI Assessment of the Viscoelastic Properties of Normal and Abnormal Breast Tissue

PRINCIPAL INVESTIGATOR: Donald B. Plewes, Ph.D.

CONTRACTING ORGANIZATION: Sunnybrook & Women's College Health Sciences Centre
Toronto, Ontario M4N 3M5, Canada

REPORT DATE: July 2000

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	July 2000	Annual (1 Jul 99 - 30 Jun 00)

4. TITLE AND SUBTITLE
MRI Assessment of the Viscoelastic Properties of Normal and Abnormal Breast Tissue

5. FUNDING NUMBERS
DAMD17-99-1-9391

6. AUTHOR(S)
Donald B. Plewes, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Sunnybrook & Women's College Health Sciences Centre
Toronto, Ontario M4N 3M5, Canada

E-MAIL:
don.plewes@swchsc.on.ca

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES
Report contains color photos

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 Words)*

The biomechanical properties of breast tissue represent an attractive property by which to detect disease and aid in differentiation between normal and benign breast tissues. Objective measurements of breast tissue biomechanical properties have been attempted in the past based on ex-vivo tissue samples. While these studies indicate large variations in breast tissue elastic modulus among various breast tissues, these data are subject to sampling errors arising from tissue heterogeneity within the tissue samples and potential differences arising from ex-vivo conditions. In this project, we aim to study these properties with an MRI method, both in-vitro and in-vivo, and assess the biomechanical properties of fat, fibroglandular and cancerous breast tissues. During our first year of funding, we have initiated the development of two uni-axial loading systems, an MRI-based imaging approach and a table-top system, for more conventional uni-axial loading measurements. In addition, we developed various inverse solution algorithms for reconstruction of elastic modulus derived from strain data acquired by MRI data. Finally, we optimized a software system for meshing that takes MRI breast images and converts them to a suitable mesh for finite element deformation analysis.

14. SUBJECT TERMS
Biomechanical, MRI, Elastography, Finite Element Analysis, Breast Cancer

15. NUMBER OF PAGES
17

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

___ Where copyrighted material is quoted, permission has been obtained to use such material.

___ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

___ Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

N/A In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

X For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

N/A In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

N/A In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

N/A In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

PI - Signature

Date 21/2000

Table of Contents

MRI Assessment of the Viscoelastic Properties of Normal and Abnormal Breast Tissue: Annual Report to the US Army

INTRODUCTION

For centuries, manual palpation to assess tissue stiffness has been used as a standard means to detect diseased tissue states. During the past several years, we[1,2] and others[3,4,5] have been exploring the use of imaging to assess the biomechanical properties of breast tissue based on MRI elastography. The subject of this proposal is to obtain a better understanding of the biomechanical properties of breast tissue as measured by MRI elastography with the potential application of aiding in improved diagnosis of breast cancer and tissue deformation analysis.

Our specific goal will be to apply MRI motion detection methods to measure tissue strain under the influence of applied stress with an external applicator. By an analysis of the resulting motions and through the use of an appropriate analysis technique, we aim to measure the distribution of tissue elastic properties in-vitro and in-vivo. A number of normal breast tissue samples and a number of breast tissue pathologies will be obtained from pathology and tissue stiffness measures obtained. Based on these data, the feasibility of predicting tissue deformation in-vivo will be tested.

RESEARCH TASKS - Year I

This project is a three-year project with a number of separate research goals and tasks. During the first year, three tasks were to be performed as follows:

Task I - To develop two instruments for measuring tissue elastic properties. The first instrument was an MR-compatible device aimed at applying periodic compression to the tissue samples to measure the resulting distribution of strain within the tissue sample with MRI for Young's modulus analysis. The second device was a table top system for measuring stress and strain in a uni-axial loading experiment in ex-vivo tissue samples.

Task II - In parallel with the development of these instruments, a second task was to develop and write inverse solution codes to analyze the distribution of strains from the MR uniaxial loading device. The output of these data was to assess tissue elastic properties from small in-vitro tissue samples.

Task III - The third task was to develop meshing algorithms to allow segmentation of breast tissue from 3D MRI images of the breast. This will be used in Years 2 & 3 to apply measures of tissue constitutive properties obtained from tissue samples to demonstrate breast tissue deformation in-vivo.

PROGRESS TO DATE:

Task I - MR Compatible Loading System

During the first year, two systems for uniaxial loading were designed and configured. The first was designed as a system for implementation in the MR scanner for imaging. The system, designed to be completely MR compatible, allows controlled compression of small tissue samples and phantoms for testing purposes. It is driven by an ultrasound stepper motor under appropriate computer control and allows cyclic compression at variable frequencies from .1 to 1.5 Hz. The amplitude of compression is controllable from 0 to 5 mm of surface formation. Adjustments of the compression apparatus allow for a stable contact on the surface of the phantom for uniform stress delivery. In conjunction with this system, an MRI pulse sequence using a stimulated echo acquisition method (STEAM)[3,6] was written and tested. A typical strain image of a phantom is shown in ***Figure 1***, along with a predicted strain image for the same phantom geometry based on Finite Element Analysis (FEA). The agreement between the two images is excellent. This system was used to measure a number of parameters between strain images as obtained by this system and that which is predicted by FEA. The general conclusion of this study is that FEA simulations of heterogeneous phantom can be accurately obtained given a knowledge of the constitutive properties of the tissue materials. This work has been submitted as a paper to *Medical Physics*.

Task I - Table Top Loading System

In parallel with these developments, a second uniaxial loading system was designed and is being configured. This system allows for bench top uniaxial loading experiments under a broad range of frequencies and amplitudes. The system is configured with a programmable, linear stepper motor that provides very accurate and stable compression of tissue samples over a broad range of frequencies from DC to approximately 30 Hz. We have configured a sensitive load cell to allow dynamic measures of stress across the sample while measuring the applied strain dynamically with position sensors. This system, still in a stage of construction and software optimization, will be used to measure the properties of tissues samples for comparison to that determined by MRI methods.

Task II - Inverse Solution Studies

The MR system will be used with some form of inverse solution to determine the distribution of tissue stiffness. We have studied this problem and developed direct inverse solutions based on Navier equations. A typical example of this is shown in ***Figure 2*** which is an inverse solution of a phantom containing a single spherical lesion. The details of the mathematics of this concept has been submitted for publication and is now in press in *Physics in Medicine and Biology*. The results of this paper show that the required displacement signal/noise ratios of the MR data must be quite high with values in excess of 1000 before reasonable images can be obtained. Ideally, SNR values in the vicinity of 5000 provide good quality inversions for tissue studies.

Task III - Meshing Algorithms

Meshing of MR data for deformation studies is an important task for this proposal. We model the breast tissues as continua and assign mechanical properties

obtained from previous experimental measurements to simulate breast tissue deformation using FEA. For breast discretization, we use MAMMOGRID: a custom-written program developed in our lab for breast FE mesh generation. This program processes MRI breast images to create 3D patient specific breast FE mesh. MAMMOGRID is capable of calculating FE meshes using two methods. One method is voxel based and leads to abrupt surfaces and tissue interfaces while the other is based on mapping and leads to smooth surfaces and tissue interfaces. We use ABAQUS: a commercial FEA to process the breast mesh and simulate the deformation. As shown in ***Figure 3***, the breast MRI image is first segmented to separate different tissues within the breast. The segmented images are then processed by MAMMOGRID to calculate the breast FE mesh shown in ***Figure 4.*** The details of this method is submitted as a manuscript to the *IEEE Transactions on Medical Imaging*.

FUTURE WORK

The proposed research as stated in the original proposal remains a valued target. Conclusions from the first year's work suggest that MRI imaging of tissue samples is feasible; however, high SNR in strain data is needed in order to assess tissue elastic modulus. We will continue to complete the development of the uni-axial loading system for bench top measurements and compare these results to that obtained with the MRI approach. The goals for Years 2 and 3 remain the same as originally proposed in our applications. We will purse alternative reconstruction methods for in-vivo and in-vitro analyses that will be practical methods to determine tissue properties for distortion studies.

KEY RESEARCH ACCOMPLISHMENTS

1) The design and construction of two uniaxial loading systems and control systems/software is well underway. The assessment of MRI measured strain data from the imaging loading system show excellent agreement with that predicted from FEA.
2) The development of an inverse solution for elasticity measurements from MRI derived strain data has been completed and a paper outlining the method is accepted for publication. This paper shows that both modulus and pressure can be directly calculated from quasi-static strain data derived from MRI although high SNR is needed to achieve stable results.
3) Segmentation and meshing of MRI breast data for deformation analysis is underway. We have developed a new meshing system (MAMMOGRID) that allows automated meshing of MRI data and provides high quality images while minimizing the number of mesh elements for future finite element analyses.

REPORTABLE OUTCOMES

During the past year, we have submitted a number of papers and symposium abstracts, as detailed below, which relate to the research contained in this project.

PUBLISHED OR SUBMITTED MANUSCRIPTS:

1) Scarrietta J, Bishop J, Samani A, Plewes DB. MRI Validation of Soft Tissue Deformation as Modeled by Nonlinear Finite Element Analysis. Submitted to Medical Physics, 2000.
2) Plewes DB, Bishop J, Samani A, Sciarretta J. Visualization and Quantization of Breast Cancer Biomechanical Properties with Magnetic Resonance Elastography. Physics in Medicine and Biology 45(6):1591-1610, 2000.
3) Samani A, Bishop J, Sciarretta J, Plewes DB. Automated 3-D Finite Element Mesh Generation Technique of Breast using MRI Data. Submitted to IEEE Transactions on Medical Imaging, July 2000.
4) Bishop J, Samani A, Sciarretta J, Plewes DB. Two-dimensional MR Elastography with Linear Inversion Reconstruction: Methodology and Noise Analysis. Physics in Medicine and Biology 45(8):2081-2092, 2000.

ABSTRACTS:

1) Sciarretta J, Bishop J, Samani A, Plewes DB. MR Validation of Soft Tissue Deformation as Modeled by Non Linear Finite Element Analysis. International Society for Magnetic Resonance in Medicine: Seventh Annual Meeting, Philadelphia, May 22-28, 1999, Paper #246.
2) Bishop J, Samani A, Plewes DB. Pressure/Modulus Inversion for MR Elastography. International Society for Magnetic Resonance in Medicine: Seventh Annual Meeting, Philadelphia, May 22-28, 1999, Paper #2164.
3) Bishop J, Samani A, Sciarretta J, Plewes DB. Use of Constraints to Produce Plane Strain Conditions for MR Elastography. International Society for Magnetic Resonance in Medicine: Eighth Annual Meeting, Denver, April 1-7, 2000, Paper #1735.
4) Samani A, Bishop J, Sciarretta J, Plewes DB. Automated Three Dimensional Finite Element Mesh Generation Technique of Patient-specific Breast Using MRI Data. International Society for Magnetic Resonance in Medicine: Eighth Annual Meeting, Denver, April 1-7, 2000, Paper #2175.
5) Samani A, Bishop J, Sciarretta, Plewes DB. Breast Magnetic Resonance Elastography: A New Reconstruction Technique Using MRI Derived Constraints. International Society for Magnetic Resonance in Medicine: Eighth Annual Meeting, Denver, April 1-7, 2000, Paper #2174.

CONCLUSIONS

To date, we have made good progress toward our end goal of understanding the constitutive properties of breast tissue and developing the means to apply these in tissue deformation analyses. The overall goal was to provide accurate mathematical tools to predict tissue deformation in the presence of compression and to determine tissue properties of various breast tissues, both normal as well as benign and neoplastic tissues. The significance of this work remains high providing a platform for new detection and diagnosis methods for breast cancer and opening up new applications of breast imaging including data fusion and therapy planning tools based on predictive tissue deformation analysis capabilities to be developed in the future years of this grant.

REFERENCES

1. Plewes DB, Betty I, Urchuk S, Soutar I. Visualizing Tissue Compliance with MR. Journal of Magnetic Resonance Imaging 5(6):733-738, 1995.

2. Bishop JB, Poole G, Leitch M, Plewes DB. Magnetic Resonance Imaging of Shear Wave Propagation in Excised Tissue. Journal of Magnetic Resonance in Medicine 8:1257-1265, 1998.

3. Chenevert T, Skovroda A, O'Donnell M, and Emelianov S. Elasticity Reconstruction Imaging by Means of Stimulated Echo MRI. Magnetic Resonance in Medicine 39: 482-490, 1998.

4. Muthupillai R, Lomas D Rossman P, Greenleaf J, Manduca A, Ehman R. Magnetic Resonance Elastography by Direct Visualization of Propagation Strain Waves. Science 26:1854-1857, 1995.

5. Sinkus R, Lorenzen J, Schrader D, Morenzen M, Dargatz M, Holz D. High-Resolution Tensor MR Elastography for Breast Tumour Detection. Physics in Medicine and Biology 45:1649-1664, 2000.

6. Plewes DB, Bishop J, Samani A, Sciarretta J. Visualization and Quantization of Breast Cancer Biomechanical Properties with Magnetic Resonance Elastography. Physics in Medicine and Biology 45(6):1591-1610, 2000.

Appendix 1: Figures for the body of the proposal

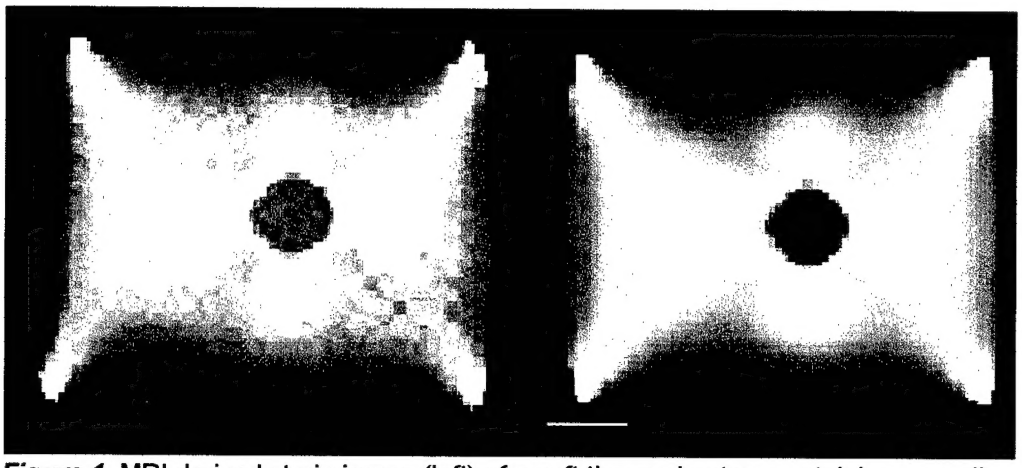

Figure 1. MRI derived strain image (left) of a soft tissue phantom containing a small hard lesion. The corresponding predicted strain image (right) from a finite element analysis uses information about the tissue properties based on the measured modulus of the component materials in the phantom. Agreement between the measured and calculated strain images is excellent.

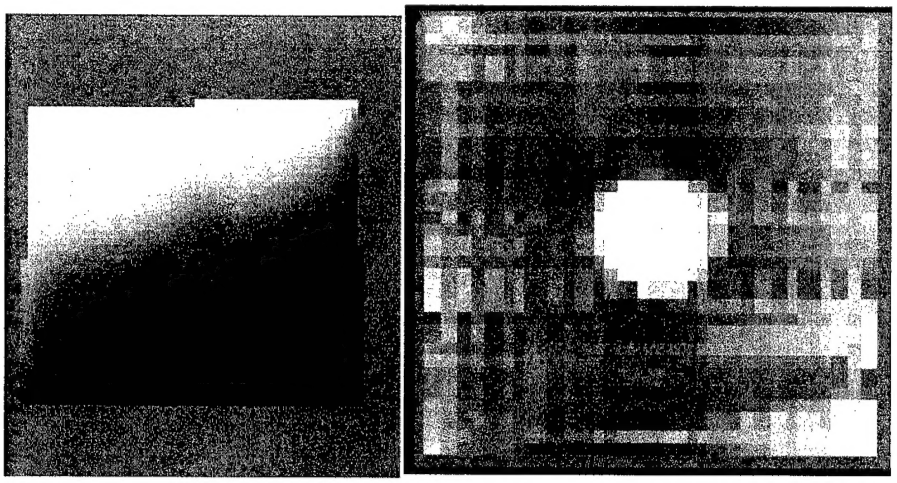

Figure 2. (Left) MRI measurements of displacement in one direction derived from a STEAM sequence in a phantom containing a small 1 cm diameter lesion. The lesion exhibited twice the modulus of the surrounding material and is visible as a slight variation in the displacement data. (Right) The corresponding calculation of tissue modulus based on a linear inversion method was developed by Bishop et al. as part of this proposal.

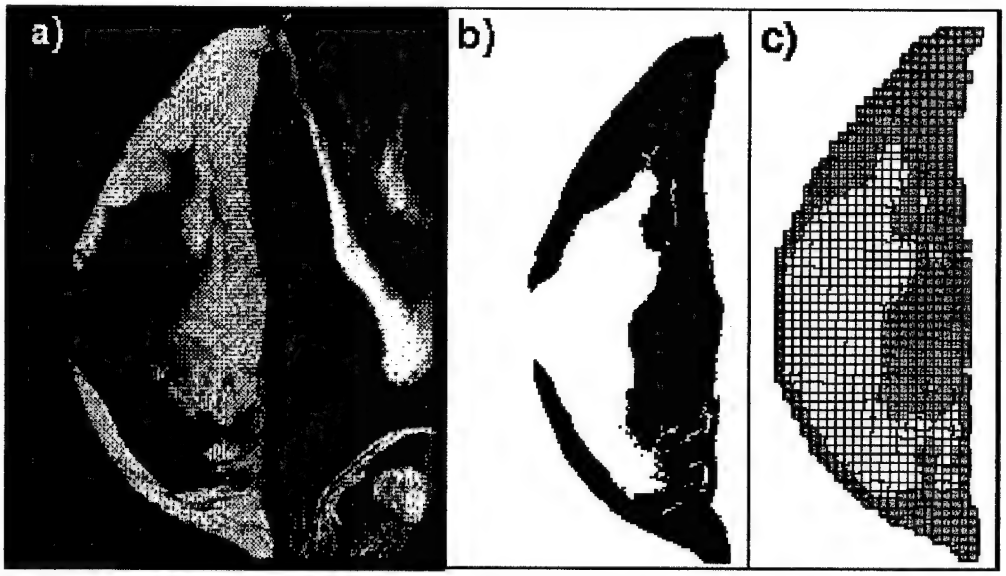

Figure 3. A breast MR image (a), corresponding segmented image (b), and FE mesh of a single slice (c).

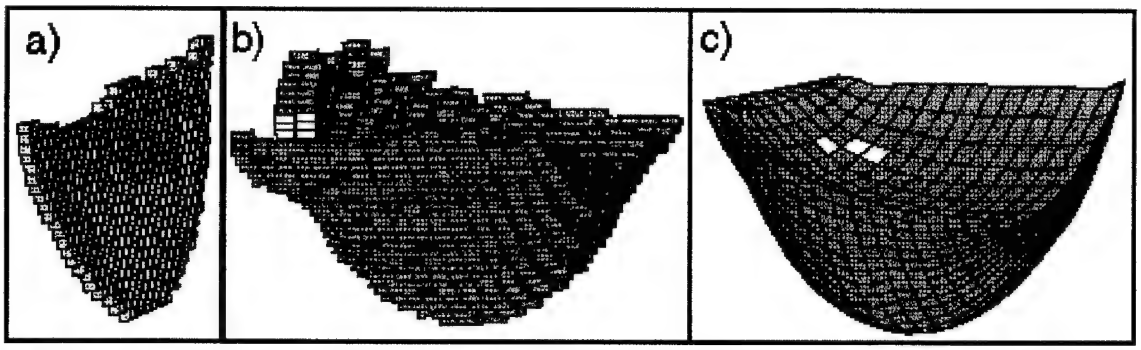

Figure 4. Calculated FE mesh of a single breast slice (a), FE mesh of the entire breast using the voxel based method (b), and FE mesh of the entire breast using the mapping method.

Appendix 2: Abstracts

1) Sciarretta J, Bishop J, Samani A, Plewes DB. MR Validation of Soft Tissue Deformation as Modeled by Non Linear Finite Element Analysis. International Society for Magnetic Resonance in Medicine: Seventh Annual Meeting, Philadelphia, May 22-28, 1999, Paper #246.
2) Bishop J, Samani A, Plewes DB. Pressure/Modulus Inversion for MR Elastography. International Society for Magnetic Resonance in Medicine: Seventh Annual Meeting, Philadelphia, May 22-28, 1999, Paper #2164.
3) Bishop J, Samani A, Sciarretta J, Plewes DB. Use of Constraints to Produce Plane Strain Conditions for MR Elastography. International Society for Magnetic Resonance in Medicine: Eighth Annual Meeting, Denver, April 1-7, 2000, Paper #1735.
4) Samani A, Bishop J, Sciarretta J, Plewes DB. Automated Three Dimensional Finite Element Mesh Generation Technique of Patient-specific Breast Using MRI Data. International Society for Magnetic Resonance in Medicine: Eighth Annual Meeting, Denver, April 1-7, 2000, Paper #2175.
5) Samani A, Bishop J, Sciarretta, Plewes DB. Breast Magnetic Resonance Elastography: A New Reconstruction Technique Using MRI Derived Constraints. International Society for Magnetic Resonance in Medicine: Eighth Annual Meeting, Denver, April 1-7, 2000, Paper #2174.

MR Validation of Soft Tissue Deformation as Modeled by Non Linear Finite Element Analysis

J. Sciarretta, J. Bishop, A. Samani, D. B. Plewes
Sunnybrook Health Science Center, Dept. of Medical Biophysics, University of Toronto, Toronto, Ontario, Canada

Introduction

Over the past decade, researchers have studied the biomechanical properties of normal and diseased tissues. In particular, Sarvazyan (1) has shown that certain types of breast cancers can exhibit a substantial increase in Young's modulus by as much as a factor of seven. While mammography and contrast enhanced MRI have been shown to have sensitivities often exceeding 90% for breast cancer, specificity remains poor. However, we hypothesize that using information on tissue stiffness will substantially improve specificity.

MR Elastography based on inverse solutions of strain images from quasi-static compression and shear wave velocity propagation have been proposed. These inverse solutions require an accurate breast tissue model which can predict tissue deformation for known boundary conditions, tissue modulus and applied stress. Thus a validation of a breast tissue model is a necessary first step in optimizing inverse solution development. Our goal is to compare the displacement field in a phantom as measured by MR to that predicted by a three dimensional finite element model.

Methods and Materials

Phantom

The phantom is a cube of gel with a stiffer cylindrical inclusion placed near the center. The dimensions are 60mm x 65.5mm x 57.4mm and the inclusion has a diameter of 12 mm and is 60 mm long. The Young's modulus of the gel and the inclusion are 8300 +/- 250 Pa and 128900 +/- 3600 Pa respectively. Both phantom materials exhibit approximately linear elastic behavior in the strain regime of 0 to 12%, with the largest deviations from linearity of 1.3% and 1.5% respectively at a strain of 12%. The elastic modulus of each sample was calculated by applying a known strain and measuring the resulting stress.

Phantom Deformation

A special purpose, computer controlled, MR compatible compression apparatus was used to provide precise, time varying compression to the phantom. The compression apparatus applied a sinusoidal modulated stress to the upper surface of the phantom during MR imaging. The maximum velocity delivered to the phantom surface was 15mm/s at .75Hz. The maximum surface displacement was 6.25 mm (11% strain).

MR Velocity and Strain Measurements

A gated CINE phase contrast pulse sequence (TR/TE - 76 ms/16ms) was used to obtain velocity measurements at 17 points evenly distributed throughout the compression cycle. The pulse sequence was triggered by the compression apparatus through the cardiac trigger. The spatial resolution was 390x780 microns with a slice thickness of 10 mm. Using a surface coil, SNR was between 80 to 110. Velocity data was obtained in the middle of the phantom for both in-plane directions. The displacement was determined by integrating the velocity fields using weighted forward and backward temporal integration based on velocity and acceleration terms.

Non Linear Finite Element Analysis

Non linear finite element analysis (ABAQUS) of the phantom was performed which allows a range of tissue models including simple linear elastic materials to non-linear, viscoelastic tissues. As a starting point, the gel was modeled as an isotropic, linear elastic material. The modeled object matched the measured phantom geometry and used the measured gel modulus values. The model assumed constant compression and did not take into account the slow cyclical nature of compression used in the MR experiment since viscous effects are thought to be minimal.

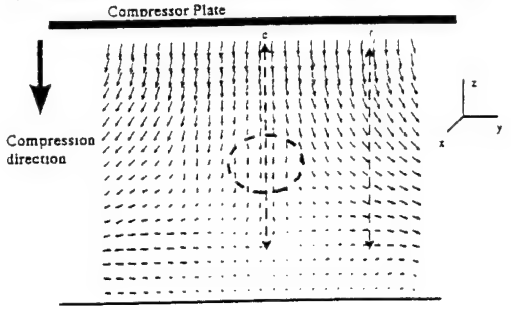

Fig. 1. Velocity field at a point in the cycle for a slice. Dashed lines represent the inclusion. V_{max} = -12 mm/s.

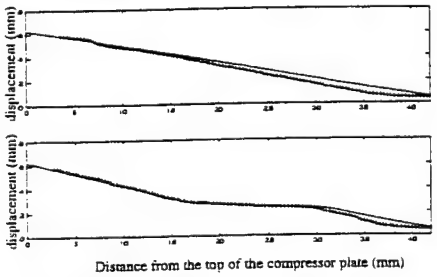

Fig. 2. Displacement along paths r and c (labeled in Fig. 1) at maximum compression. Solid lines represent the displacements calculated by the Finite element analysis and crosses represent the experimental data.

Results

Based on time varying displacement images, clear rendering of the phantom inclusion was evident. Deformation determined from the finite element analysis agreed with MR data, although agreement was not perfect. Discrepancies likely arise due to the boundary conditions to the top of the phantom, which was modeled as constant compression, as well as a small velocity offset caused by eddy currents affecting displacement calculation near the bottom of the phantom. Nevertheless, this shows that finite element modeling based on simple material constitutive properties can provide accurate assessment of large deformations of tissue equivalent materials.

Conclusion

Non linear finite element modeling of tissue equivalent gels provides an accurate estimate of tissue deformation with strains up to 11%. Errors arising from the cyclic nature of the MR experiment need further consideration. Ongoing studies with real tissue samples based on this type of experiment will be the subject of future work to further access the validity of finite element analysis for elastography inverse solutions.

References

(1) A. Sarvazyan et al, Proceedings of International Workshop on Interaction of Ultrasound with Biological Media, (1994).

Pressure/Modulus Inversion for MR Elastography

J. Bishop, A. Samani and D.B. Plewes
Department of Medical Biophysics, University of Toronto

Introduction Tissue contrast based on elastic properties has significant potential in imaging for breast cancer and other disease [1]. Since MR imaging is not directly sensitive to tissue elastic properties, quantities such as shear modulus must be calculated from measurements of displacement.

In incompressible tissues, the scalar pressure field is an additional unknown quantity which has spatial variation. Knowledge of the pressure field, combined with the elastic modulus, would permit a stress analysis of the tissue in question. From a biomechancial perspective, knowledge of stress and force is very important. In this work, simulations are presented which illustrate the potential for simultaneous inversion of pressure and elastic modulus from a known displacement field.

Methods The vector equation describing static equilibrium in a linearly elastic material is:

$$\nabla p + \nabla(\mu \nabla \mathbf{u}) = 0 \qquad (1)$$

where p is scalar pressure, μ is the elastic modulus, and u is the vector displacement field that is measured with phase contrast MRI. Pressure may be eliminated analytically from these equations with the use of a third differential operation as shown by [2]. However, we retain p as an unknown, such that derivatives of the displacement vector field are limited to second order; this may potentially improve the conditioning of the inversion matrix.

If pressure and modulus are both available, then the stress analysis of the tissue can be performed according to:

$$\mathbf{T} = p\mathbf{I} + 2\mu\mathbf{E} \qquad (2)$$

where T and E are the stress and strain tensors respectively.

A simulated two-dimensional displacement field was created for a Gaussian shaped object contained in a square FOV. Normally distributed random values were added to simulate a maximum SNR of 200 in the displacement data. Low pass filtering by sinc convolution was applied to smooth the effects of noise prior to inversion. The boundary conditions for the inversion were assigned to be constant pressure and constant elastic modulus. The solution of equation 1 was performed with a finite difference numerical method.

Results Inverted pressure and modulus are plotted in figures 1a-b, and may be compared to the true values shown in c-d. In graphs e-f, line profiles through the centre of the above images are plotted to demonstrate quantitatively the performance of the inversion. These results indicate that the quality of the modulus reconstruction is similar to that for pressure. However, the pressure reconstruction is more sensitive to noise as SNR is reduced.

Conclusions We have demonstrated with simulations that pressure can be retained as an unknown variable and solved for along with elastic modulus in a linear inversion procedure. Retaining pressure as an unknown has two potential advantages: a third spatial derivative of the displacement data is unnecessary, and a stress analysis of the tissue may subsequently be performed if desired.

The combined pressure/modulus inversion is still somewhat ill-conditioned since noise perturbations to the raw displacement data on the order of 10^{-4} cause some instability to appear in the solution. With moderate filtering however, the SNR required in the displacement data is within practical limits for MRI acquisition. Use of standard regularization methods to better manage this ill-conditioning will be discussed. The sensitivity to noise perturbation also suggests that it may not be possible to reconstruct sharp-edged features in the modulus distribution by this method.

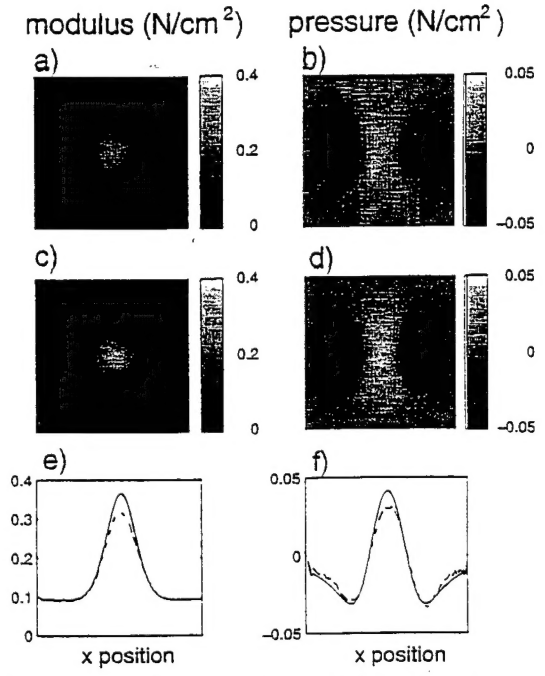

Figure 1. Results of the pressure/modulus inversion corresponding to unfiltered SNR=200 in the displacement data. Figures 1a-b show the modulus and pressure reconstructions, while figures c-d show the true modulus and pressure fields. Horizontal profile plots through the above images are shown in e-f for the calculated quantities (- - -) and true quantities (——).

References

[1] Sarvazyan A, Goukassian D, and Maevsky G. *et al. in* "Proceedings of International Workshop on Interaction of Ultrasound with Biological Media", pp. 69–81. Valenciennes, France, 5-9 April 1994.

[2] Chenevert T, Skovoroda A, O'Donnell M, and Emelianov S. *Magn. Reson. Med.* 1998; 39:482–490.

Use of Constraints to Produce Plane Strain Conditions for MR Elastography

J. Bishop, A. Samani, J. Sciarretta and D.B. Plewes
Department of Medical Biophysics, University of Toronto

Introduction Tissue contrast based on elastic properties has significant potential in imaging for breast cancer and other disease [1]. Since MR imaging is not directly sensitive to tissue elastic properties, quantities such as shear modulus must be calculated from measurements of displacement.

In general, tissues will deform in three dimensions during MR elastography (MRE). In order to reconstruct elastic modulus by an inverse method, 3 components of displacement must be acquired in order to establish a boundary value problem for numerical solution. Many investigators have assumed two-dimensional plane-strain conditions to analyze MRE displacement data, but it has been noted that such approximations are not very accurate for spherical inclusions [2].

However, an approximate state of plane strain can be achieved by physically constraining the material in one dimension. With simulations and experiments, we demonstrate that MRE data acquisition and analysis can be conducted in two dimensions through the use of external constraints.

Methods Simulations were conducted with a cubic object containing a spherical inclusion of modulus 2.5 relative to background. This object was discretized on a 48x48x48 mesh. A compression of 10% was simulated for with lateral constraints applied to the x_3 direction. A three-dimensional inclusion phantom was constructed from plastisol PVC (M-F Manufacturing Company, Fort Worth TX), with inclusion modulus ratio similar to that of the simulation. The phantom was placed in a MR-compatible compressor device driven by an ultrasonic motor (USR60-N4, Shinsei Corp., Tokyo Japan). Panels were positioned to constrain this object in the x_3 direction, and the motion was measured in unconstrained directions with a stimulated-echo phase contrast method [3].

Results Figure 1 shows results in the central $x_1 - x_2$ plane of the three-dimensional simulation, with constraint in the x_3 direction. The strain in the restricted direction (1c) is near zero, as clearly seen in the accompanying x_1 profiles (1d). Figure 2 shows corresponding experimental results in the same orientation. Although e_{33} was not measured experimentally, $e_{11}+e_{22}$ (2c) is a good approximation since plastisol is an incompressible material having Poisson's ratio $> .499$ [4]. The profiles in figure 2d show good qualitative agreement with the features of figure 1d.

Conclusions Many investigators have identified the goal of solving a three-dimensional modulus distribution with accompanying 3D displacement data set. However, even a low-resolution 3D reconstruction is a challenging numeric problem and data acquisition requirements are substantial. As an alternative, we have demonstrated with phantoms made of incompressible materials that confinement techniques may be used to produce very good plane-strain conditions, such that measurement and analysis can be conducted in two dimensions. Implementation of in-vivo confinement in breast MRE is envisioned with the chest wall as one of the constraints.

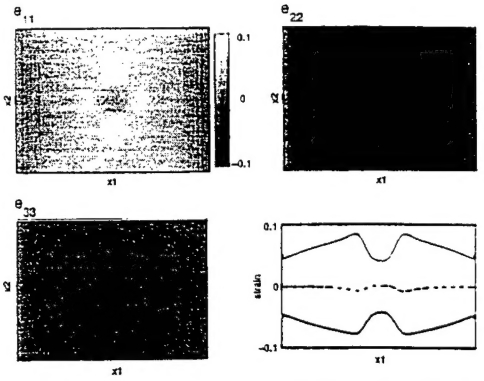

Figure 1 a-c) Simulated strain components. d) x1 profiles of e_{11} (——), e_{22} (——), and e_{33} (– – –).

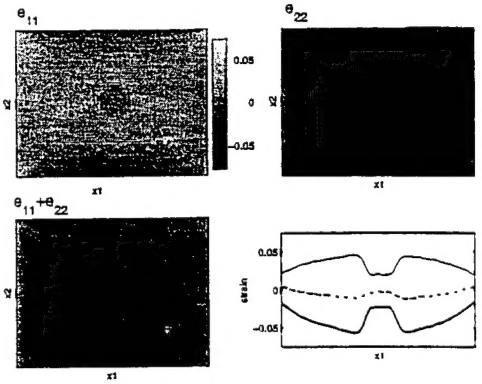

Figure 2 a-c) Experimental strain components. d) x1 profiles of e_{11} (——), e_{22} (——), and $e_{11} + e_{22}$ (– – –).

References

[1] Sarvazyan A, Goukassian D, and Maevsky G. *et al.* Elasticity imaging as a new modality of medical imaging for cancer detection. *in* "Proceedings of International Workshop on Interaction of Ultrasound with Biological Media", pp. 69–81. Valenciennes, France, 5-9 April 1994.

[2] Bilgen M and Insana M. Elastostatics of a spherical inclusion in homogeneous biological media. *Phys. Med. Biol.* 1998; **43**:1–20.

[3] Chenevert T, Skovoroda A, O'Donnell M, and Emelianov S. Elasticity reconstructive imaging by means of stimulated echo MRI. *Magn. Reson. Med.* 1998; **39**:482–490.

[4] Erkamp R, Wiggins P, Skovoroda A, Emelianov S, and O'Donnell M. Measuring the elastic modulus of small tissue samples. *Ultra. Imag.* 1998; **20**:17–28.

Automated Three Dimensional Finite Element Mesh Generation Technique of Patient-specific Breast Using MRI Data

A. Samani, J. Bishop, J. Sciarretta, D. Plewes
Department of Medical Biophysics, University of Toronto

Introduction Predicting breast tissue deformation is of great significance in various medical applications. In lumpectomy, the tumor must be located accurately before the operation. Locating the tumor is done using imaging techniques which are performed under tissue configuration of compression or body position that is often entirely different from that of the surgery. In this case tissue deformation resulting from the new tissue configuration or body position must be determined to correct the tumor location. In multi-modality imaging of the breast, data fusion can be successful only when images are represented in an equivalent configuration. This equivalent representation can be achieved by calculating the tissue displacements resulting from the mechanical effects applied on the breast in different modalities [1]. In breast biopsy, the biopsy needle causes tissue deformation which leads to tumor displacement. This deformation can be calculated to determine the aiming angle required for a successful biopsy. The finite element method (FEM) has been successfully used in modeling the mechanical behaviour of biological tissues such as bone and myocardium. This work is aimed at using FEM in modeling breast tissue deformation. The first step in FEM is mesh generation which is, especially in large and geometrically complex object, the most tedious and time consuming step in FEM. This article presents an efficient method of generating three-dimensional meshes of heterogeneous objects with complex geometry, e.g. the breast, using MRI data.

Methods The method uses MR images to create the FEM mesh. It is capable of processing axial, coronal or sagittal images to produce the mesh. Unlike other methods [2], no user interaction is required to extract the boundaries of the breast. Furthermore, the breast is considered to be composed of adipose, fibroglandular tissue and skin. A signal intensity based segmentation algorithm is used to separate the adipose and fibroglandular tissue in the MR images. The segmented images are imported to a custom-written program which produces a FEM input file compatible with commercial FEM softwares such as ABAQUS. In the meshing program, eight noded hexahedral elements are chosen to construct the adipose and fibroglandular tissue while four noded membrane elements are used used to model the skin. For node generation, the nodes are arranged in the form of a 3-d rectangular lattice which confines the breast volume. For element generation, the boundary of each slice is found by searching the image row by row. A boundary point is located once an adipose voxel is reached. These points are stored and later used in element generation. Elements in each slice are generated and then stacked to reconstruct a complete 3-d mesh. Skin elements are generated by identifying the outer face of elements on the breast surface. Finally, to have a better geometry representation, a smoothing technique [3] is used to obtain a relatively smooth surface and material interfaces.

Results To validate this meshing technique, an agar phantom which consists of a block of agar (2%) with a hard cylindrical inclusion was made. This phantom was scanned and a set of axial MR images were acquired using a GE SIGNA 1.5 T scanner. These images were segmented and then processed by the meshing program. As a result, a FE mesh was obtained after resolution reduction by a factor of 4. This mesh along with another mesh which was created manually are shown in Figure 1. Assuming that the phantom undergoes 4 mm compression, displacements were calculated by applying the FEM to these meshes. The results indicate that there is a maximum difference of 6% between the nodal displacements.

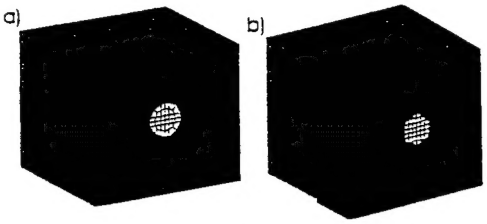

Figure 1: Manually created a) and calculated b) 3D mesh.

To test this technique in a more realistic application, sagittal MR images of a breast from a healthy volunteer was acquired using a spin-echo pulse sequence. These images were segmented and processed by the meshing program to produce a mesh of 16,841 elements and 15,939 nodes after resolution reduction by a factor of 4 in the sagittal plane directions. An MR image of a sagittal slice of the breast and the 3-d finite element mesh of the breast excluding the skin are depicted in Figure 2.

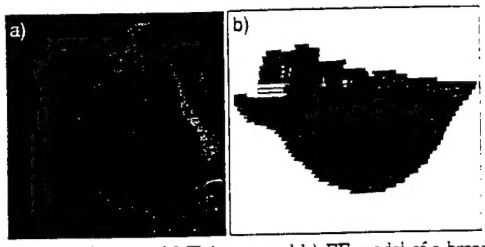

Figure 2: a) Sagittal MR image and b) FE model of a breast.

Conclusions The presented technique offers an efficient, automated means of generating three-dimensional finite element meshes from MR images. The technique, without any user intervention, is capable of reproducing delicate anatomic features of complex organs such as the breast. Unlike other strategies, this technique does not require manual determination of contours defining boundaries of each relevant structure in every planar image. In this technique the breast is considered to be composed of adipose, fibroglandular tissue and skin. The results demonstrate that this technique is capable of generating meshes of large and geometrically complex organs with a reasonable accuracy. Therefore, it can be effectively used in 3-d FE modeling of breast tissue deformation.

References

[1] Samani A. *et al. 23rd ASB Annual Meeting* 1999.

[2] Azar F. S. *et al. 7th Scientific Meeting of ISMRM* 1999.

[3] Camacho D. L. A. *et al. Biomechanics* 1997; 30(10):1067–1070.

Breast Magnetic Resonance Elastography: A New Reconstruction Technique Using MRI Derived Constraints

A. Samani, J. Bishop, J. Sciarretta, D. Plewes
Department of Medical Biophysics, University of Toronto

Introduction It is well known that variations in tissue elastic properties are associated with the presence of cancer [1]. Studies [1] suggest a 15 fold increase in the stiffness of breast cancer compared to normal fibroglandular tissue while fibroadenomas were only a factor of two stiffer than normal breast parenchyma. These observations stimulated the development of imaging techniques aimed at imaging tissue elastic modulus in a quantitative manner. In these techniques, some form of external mechanical actuation is used to compress tissues. Imaging methods are used to measure the resulting deformation, from which the tissue elastic modulus can be subsequently calculated. This article presents a new quasi-static magnetic resonance elastography (MRE) reconstruction technique in which the geometry of tissues is assumed to be known *a priori*. While other investigators such as [2] assume no knowledge on tissue distribution, in this method we assume that the geometry of the breast tissues is known from a contrast-enhanced MRI scan. This knowledge provides a set of constraints which leads to a straight forward iterative inversion technique.

Methods We constructed a reciprocating compression device designed to deliver quasi-static compression of $0 - 5$ mm amplitude at the surface of cubical phantoms at a frequency of 1.0 Hz. This device is driven sinusoidally by a MR compatible ultrasonic motor and the resulting deformation is measured using a stimulated echo (STEAM) pulse sequence. For modulus reconstruction, we implement an iterative process whereby a current estimate of modulus distribution is used to calculate the stresses resulting from the compression. The stress field, combined with a measured strain component, e.g. ϵ_{zz}, is then used to update the Young's modulus distribution using Hooke's law for incompressible materials:

$$E = \frac{1}{\epsilon_{zz}}(\sigma_{zz} - 0.5\sigma_{yy} - 0.5\sigma_{zz}) \qquad (1)$$

For breast elastograpy, the breast is assumed to be placed between two parallel plates which exert compression at low frequency. This compression is modeled through a static finite element (FE) contact problem model as described in [3]. At each iteration, stresses are calculated and used to update E through equation 1. The modulus of each tissue is calculated by averaging over the area of the tissue which is determined from a contrast-enhanced MRI scan. Furthermore, to avoid undesirable nonlinear behaviour of noise, averaging is performed on Young's modulus reciprocals. The reciprocal of the obtained average of each tissue is then used as the updated modulus of the tissue.

Results This technique was first applied to a plastisol PVC phantom composed of a cylindrical inclusion of 1.25 cm radius surrounded by a $6 \times 6 \times 6$ cm block. Based on uniaxial experiments, E is 37.5 kpa and 11.6 kpa for the inclusion and the block respectively. The phantom was placed in a compression device driven by the ultrasonic motor and underwent a quasi-static sinusoidal compression of 4.3 mm amplitude. A STEAM puise sequence with $TR/T/TE = 1000/250/13$ ms was used for measuring the displacements in the vertical direction. A strain image of a central part of the phantom obtained from these measurements is shown in Figure 1. Based on this image the modulus ratio of the inclusion to the block is 1.87. This values was used to start the process and after 6 iterations, convergence was achieved at a ratio of 3.54 which suggests 9.5% error. A strain image calculated based on the reconstructed values is shown in Figure 1 which indicates a good agreement. To test this technique in a more realistic application, we used a 3-d FE model of a breast with a simulated lesion. A saggital slice of this FE model is depicted in Figure 1.

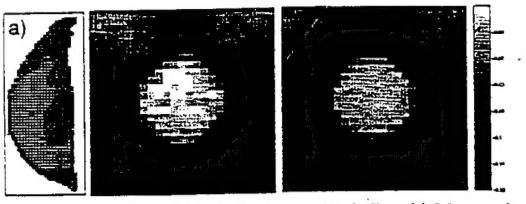

Figure 1: a) FE model of a breast sagittal slice. b) Measured strain image. c) Calculated strain image.

E of the fat, fibroglandular tissue, tumor and skin was assumed to be 2.0 kpa, 10.0 kpa, 50.0 kpa and 25.0 kpa respectively. A 5 mm compression normal to the sagittal plane was simulated, and the displacement component in the compression direction was calculated and then polluted by noise to simulate SNR of 1000 and 300. After 6 iterations, the process converged to the results summarized in Table 1. These results indicate that with SNR of 1000, the maximum error is 14.8% while SNR of 300 leads to relatively accurate reconstruction of the normal tissue moduli but inaccurate reconstruction of the tumor modulus. This inaccuracy is due to the small number of elements involved in the tumor which renders the averaging process less effective. This suggests that increasing the FE mesh resolution leads to more accurate results.

Table 1: Reconstruction results of the breast.

Iter. #	SNR	Fat	Fib.	Tumor
0	1000	2.5	3.0	6.3
6		2.0	10.0	57.4
0	300	2.5	7.6	16.0
6		2.1	10.6	93.9

Conclusions This article presents a new breast MRE reconstruction technique based on *a priori* information obtained from previous contrast-enhanced MRI. Compared to other elastography techniques, this technique is not only less demanding in terms of data acquisition and computation but also more accurate and less sensitive to noise. Through a real and simulated experiment, we have demonstrated that this technique is an encouraging candidate for future clinical applications.

References

[1] Sarvazyan A. P. *et al.* in "Proceedings of International Workshop on Interaction of Ultrasound with Biological Media", pp. 69–81.

[2] Skovoroda A. R. *et al. IEEE Trans. UFFC* 1995; 42:747–765.

[3] Samani A. *et al. 23rd ASB Annual Meeting* 1999.